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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/952,741	HATADA ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on April 22, 2004 has been entered.

Amendment filed April 22, 2004 canceling claims 2-7, 12, 13, 15, 16 and 20-24 and adding claims 25-43 has been entered.

Responsive to the RCE submission and amendment filed 22 April 2004, the Final Office action mailed April 29, 2004 is hereby vacated. The period for reply to the instant Office action starts from the mailing date of this Office action.

Claims 25-43 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claim 34 is drawn to "An isolated DNA molecule encoding a protein exhibiting alkaline α-amylase activity at a pH optimum of 8-9 produced by a polymerase chain reaction using at least one of the primers selected from the group of SEQ ID NO: 10, SEQ ID NO:7, SEQ ID NO: 3, SEQ ID NO: 6, SEQ ID NO: SEQ ID NO: 8, SEQID NO: 4, and SEQ ID NO: 11 wherein said isolated DNA molecule is isolated from a member selected from the group consisting of *Bacillus* sp. A-40-2, *Bacillus* sp. NRRL 8-3881, *Streptomyces* sp. KSM-9, *Bacillus* sp. H-167, *Bacillus* alkalothermophilus A3-8, and *Natronococcus* sp. Ah-36". Claims 35-43 depend from claim 34 and recite additional properties of the encoded alkaline α-amylase. Applicants indicate support for claim 34 "at page 2, lines 7-22" (Remarks of April 22, 2004, page 8). The indicated lines disclose that "alkaline α-amylases and alkali-resistant α-amylase[,] include an enzyme produced by" the source recited in claim 34. Applicants further indicate that "Support for new claims 35-41 can be found in claim 30. Support for new claim 42 in claim 25" (*ibid*). The Examiner is unable to locate adequate support in the specification for a DNA encoding enzymes from the recited sources, moreover comprising the recited sequences. Furthermore, support for additional limitations in claims 35-42, Applicants find in the claims that are also new. The combination of the recited enzymological properties characterize the alkaline α-amylase from

Bacillus sp. KSM-AP1378, i.e. the α-amylase of the instant invention. There is no indication that an alkaline α-amylase from any of the recited sources, if exists, has some or all of the enzymological properties of the α-amylase of the instant invention recited in the claims. Thus, there is no indication that a DNA encoding an alkaline α-amylase from the recited bacteria, including a DNA encoding an alkaline α-amylase with the specific recite properties was within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 34-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 34-43 are drawn to "An isolated DNA molecule encoding a protein exhibiting alkaline α-amylase activity at a pH optimum of 8-9 produced by a polymerase chain reaction using at least one of the primers selected from the group of SEQ ID NO: 10, SEQ ID NO:7, SEQ ID NO: 3, SEQ ID NO: 6, SEQ ID NO: SEQ ID NO: 8, SEQID NO: 4, and SEQ ID NO: 11 wherein said isolated DNA molecule is isolated from a member selected from the group consisting of *Bacillus* sp. A-40-2, *Bacillus* sp. NRRL 8-3881, *Streptomyces* sp. KSM-9, *Bacillus* sp. H-167, *Bacillus* alkalothermophilus A3-8, and *Natronococcus* sp. Ah-36".

PCR requires a pair of primers that can amplify the target nucleotide sequence. A pair of primers will amplify different DNA, if it exists, that is a target DNA for said specific pair of primers. Therefore, the claims are drawn to a genus of DNAs encoding an alkaline α-amylase with a pH optimum of 8-9 having different structures and properties. No DNA, including a DNA encoding an alkaline α-amylase with a pH optimum of 8-9, from any of the recited sources is disclosed.

The specification fails to provide any structure: function correlation present in all members of the claimed genus.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Claims 34-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA of SEQ ID NO:1 encoding an alkaline liquefying α-amylase having a pH-optimum at pH 8-9 amplified from *Bacillus* sp. A-40-2, *Bacillus* sp. NRRL 8-3881, *Streptomyces* sp. KSM-9, *Bacillus* sp. H-167, *Bacillus* alkalothermophilus A3-8, or *Natronococcus* sp. Ah-36", if it exists, does not reasonably provide enablement for a DNA encoding an alkaline liquefying α-amylase having a pH-optimum at pH 8-9 amplified using one or any pair of primers selected from SEQ ID NOs: 3-11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are broader than the enablement provided by the disclosure with regard to the huge number of all possible nucleic acid sequences encoding alkaline liquefying α-amylases having the specific desired characteristics.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The nature and breadth of the invention of claims 34-43 encompass any nucleic acid sequence having an unknown identity to SEQID NO:1 and encoding an alkaline liquefying α-amylase having a pH optimum of 8-9.

The state of the art teaches that the starting material for a PCR is DNA that contains the sequence to amplified. For a PCR, the primers are chosen to flank the region of DNA that is to be amplified. Therefore, one of ordinary skill in the art would require guidance as to which two sequences should be chose as primers. Knowing the structure of SEQ ID NO:1 it is possible to amplify the same or highly homologous sequence. However, only one specific sequence does not allow the amplification. The prior art teaches the DNAs encoding alkaline liquefying α-amylases from *Bacillus* sp. #707 and *Bacillus licheniformis*, respectively (Tsukamoto et al. and Yuuki et al., respectively, form PTO-1449 filed September 28, 1998). The DNAs disclosed by Tsukamoto et al. and Yuuki et al.

encode the amino acid sequences which have about 87% and 69% identity to SEQ ID NO:2, respectively. The disclosed α-amylases have properties different from the α-amylase of the instant invention. In particular, said α-amylases do not have pH optimum at pH 8-9 (see, for example, Response under 37 CFR 1. 116 filed January 14, 2000, pages 7-8). However, it is possible to amplify said α-amylases using a single primer and an unknown primer or possibly a pair of primers selected from SEQ ID NOs:3-11. Therefore, the prior art renders it highly unpredictable as to what are the amino acid or nucleotide sequences encoding α-amylases present in the recited bacteria.

Thus, obtaining by a PCR an alkaline liquefying α-amylases with desired characteristics is well outside the realm of routine experimentation and predictability in the art of success is extremely low. One of ordinary skill in the art would require additional guidance, such as information regarding the structure of α-amylases in the recited bacterial sources and a pair of primers to be used for the amplification. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claims 34-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ the bacterium of *Bacillus* sp. A-40-2, *Bacillus* sp. NRRL 8-3881, *Streptomyces* sp. KSM-9, *Bacillus* sp. H-167, *Bacillus* alkalothermophilus A3-8, and *Natronococcus* sp. Ah-36. Since the bacteria are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed bacteria are not fully disclosed, nor have been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the bacterial strains. The specification does not disclose a repeatable process to obtain the bacteria and it is not apparent if the bacteria are readily available to the public. Accordingly, it is deemed that a deposit of these bacterial strains should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25, with dependent claims 26-33, recites "An isolated DNA molecule encoding a protein exhibiting alkaline liquefying α-amylase activity at a pH optimum of 8-9 and possessing an amino acid sequence which has been obtained by modifying an amino acid sequence described in SEQ ID NO:2 in a manner in which one amino acid is substituted, deleted, or inserted without changing enzymological properties of said amino acid sequence described in SEQ ID NO:2 and hydrolyzes l,4-α-glucosidic linkages in starches, amylose, amylopectin, and degradation products thereof and in amylose forms: glucose

(G1), maltose (G2), maltotriose (G3), maltotriose (G4), maltopentose (G5) and maltohexose (G6) and does not hydrolyze pullulan". It is unclear which enzymological properties are encompassed by the claim other than being an alkaline liquefying α-amylase having a pH optimum at pH 8-9 and having the recited substrate specificity. Furthermore, "enzymological properties" cannot belong to a sequence but belong to a molecule. Furthermore, it is unclear what is defined by "(G1)" ,"(G2)","(G3)", etc.

Claim 26 is unclear as reciting "a nucleotide sequence for regulating expression of a DNA operatively linked to the DNA molecule" (emphasis added). Further, the difference in scope of claims 26 and 28 is unclear because the DNA of claim 26 must be recombinant.

Claim 30 recites the specific properties of the mutant alkaline liquefying α-amylase. Properties such as pH optimum recited in the independent claim 25 does not need to be repeated. Further, the claim is unclear because the enzyme is active in a pH range of 5.0 to 11.0 while it is stable in a narrower range of 5.0 to 10.5. it appears that if an enzyme is unstable, it is inactive. Further, said ranges depend on conditions such as temperature, substrate, buffer, etc. In addition, the conditions under which the enzyme "is stable" are divided in two parts that are separated by different properties. A temperature range depends on pH, for example. The stability in the presence of cations depends on conditions such as temperature, pH, etc.

Furthermore, the claim is confusing because the claimed enzyme cannot have a MW of less than 50 kD.

Claims 31-33 repeat properties recited in claim 25.

With regard to claim 33, the sequence of SEQ ID NO:3 is recited twice.

Claim 34, with dependent claims 35-43, is unclear as reciting a DNA molecule isolated from "a member selected from the group consisting of" where it appears "a bacterium" or "a strain", for example, is intended (emphasis added). Furthermore, the non-consecutive sequence in which the sequence identifiers are recited is confusing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

August 6, 2004